Review Article

Mehmet C. Yildirim, Hatice S. Ekici, Jemima Collins, Jessica Piasecki, Rob Skelly, Adam L. Gordon and Bethan E. Phillips*

Effectiveness of aerobic exercise interventions on balance, gait, functional mobility and quality of life in Parkinson's disease: an umbrella review

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Abstract

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder with increasing prevalence into older age. Aerobic exercise (AE) is the most commonly prescribed exercise for PD, although an optimal protocol is undefined. This umbrella review aimed to summarise and synthesize existent evidence regarding the effectiveness of AE on balance, gait, functional mobility, and QoL in people with PD.
Content: Six databases were searched for systematic reviews reporting the effects of AE on balance, gait, functional mobility, and QoL in people with PD from inception to June 2024. Quality of evidence was assessed using the AMSTAR-2 tool. From 4182 records, 17 systematic reviews were included for qualitative analysis. Most (n=12) were rated as critically low for methodological quality, with four rated low and one high. Moderate intensity was the most commonly investigated AE intensity (n=4), although almost half of the reviews (n=8) did not report intensity. AE protocols lasted from 1 to 64 weeks and 1 to 7 days per week. Session length was between 20 and 120 minutes. Reported outcomes included gait (n=15), QoL (n=14), balance (n=12), and functional mobility (n=7). AE does improve aspects of gait, balance, and functional mobility in PD; however it does not appear to improve QoL.
Summary and Outlook: AE is recommended as part of rehabilitation for people with PD. However, research exploring the efficacy of AE assesses multiple modalities with varied protocols. Further research is needed to identify AE protocols that will best alleviate the symptoms of PD, providing an evidence base for effective clinical translation.

Keywords: Parkinson's disease; aerobic exercise; quality of life; older people; umbrella review; balance

Adam L. Gordon and Bethan E. Phillips Co-senior authorship.

***Corresponding author: Prof. Bethan E. Phillips**, Centre of Metabolism, Ageing and Physiology (CoMAP), Academic Unit of Injury, Recovery and Inflammation Sciences (IRIS), School of Medicine, University of Nottingham, DE22 3DT, Derby, UK, E-mail: Beth.phillips@nottingham.ac.uk. https://orcid.org/0000-0002-1430-1870
Mehmet C. Yildirim and Hatice S. Ekici, Academic Unit of Injury, Recovery and Inflammation Sciences (IRIS), School of Medicine, University of Nottingham, Derby, UK
Jemima Collins and Adam L. Gordon, Academic Unit of Injury, Recovery and Inflammation Sciences (IRIS), School of Medicine, University of Nottingham, Derby, UK; and Department of Medicine of the Elderly, University Hospitals of Derby and Burton NHS Foundation Trust, Royal Derby Hospital, Derby, UK
Jessica Piasecki, Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK
Rob Skelly, Department of Medicine of the Elderly, University Hospitals of Derby and Burton NHS Foundation Trust, Royal Derby Hospital, Derby, UK

Introduction

Parkinson's disease (PD) is a chronic, progressive, neurodegenerative movement disorder [1]. The onset of PD before the age of 50 is rare but does become more common as people age [2]. Approximately 1 % of adults over the age of 60 and 4 % of those over 85 suffer with PD [3]. The motor signs of PD include tremor, bradykinesia, postural instability, and rigidity, and abnormalities in gait, balance, eye movement, posture, speech, and facial expressions [4, 5]. Of these motor symptoms, balance, gait, and mobility have been identified by people living with PD as the most important research priorities [6]. Furthermore, people with PD frequently experience non-motor symptoms such as pain, anxiety, depression, dementia, and constipation [7]. Collectively, all of these symptoms lead to deterioration in ability to perform activities of daily living (ADLs), functional independence, motor performance [8, 9], and ultimately quality of life (QoL).

Medications are the mainstay of PD treatment but cannot be offered to all people with PD due to significant adverse effects including hallucinations, confusion, motor fluctuations, dyskinesias, oedema, sudden sleep attacks, and stroke [10, 11]. Further, some PD motor symptoms and most non-motor symptoms are resistant to medication [12]. Therefore, for most people with PD exercise is regarded as a valuable component of a multimodal approach that is proposed as an effective tool in the management of PD [13]. Exercise has been shown to improve symptoms of PD, postulated to be linked to neuroprotective effects on the nigrostriatal pathway via increases in serum urate, increased release of neurotrophic factors (e.g. BDNF, GDNF), greater synaptogenesis, and reduced neuroinflammation [14, 15]. These effects of exercise may provide people with PD increased dopamine release, less striatal dopamine loss, and possible preservation of dopaminergic neurons and dopamine terminals [15]. For example, one study has shown that exercise may improve grey matter volume and cortical motor excitability, each of which have been linked to behavioural improvements [16]. Moreover, a separate clinical trial revealed that three months of aerobic exercise (AE) boosted dopamine release in the anterior striatum, suggesting that AE may improve anterior striatal function [17]. Along with improved motor control, AE has also been shown to be effective in increasing cognitive function in people with PD by lowering anti-saccade error rates, raising pro-saccade amplitudes, and improving functional connectivity between the right frontoparietal and the right dorsolateral prefrontal cortex [18]. AE is the most common exercise type prescribed for people with PD and is recommended in both American and European guidelines [12, 19, 20] as a means to possibly improve gait, aerobic capacity, functional mobility, and motor symptoms [21–24]. Some trials support that AE may also benefit lower limb strength and flexibility [25, 26]. Moreover, AE has been also shown beneficial for improving mood, cognition, depression, sleep, and fatigue in people with PD [27, 28].

Although the effectiveness of AE on PD has been previously studied, from the existing literature it is challenging to understand how different AE protocols impact specific physiological parameters and symptoms in people with PD. Previous reviews vary widely in the included exercise prescription, participant characteristics, and outcome measures; all of which hinder collective interpretation. For example, the review by Rodríguez et al., investigated the effects of only vigorous AE on people with PD [29], whilst that by Li et al., focussed on moderate-intensity AE only [30]. Further, previously published systematic reviews have variable inclusion criteria across multiple studies [31, 32]. To date, the literature offers only one umbrella review that looked at the effects of physical exercise on people with PD [33]. This large umbrella review included 139 systematic reviews across all exercise types (AE, resistance, sensory motor, combined, and any other exercise type) on any outcome related to PD, an approach which prevented the authors from making a detailed analysis of the effects of AE on PD. This review did not compare how different intensities or types of AE effect different outcomes in PD and there was no analysis as to whether AE is more beneficial (when compared with other exercise types) to ameliorate individual domains of PD. Therefore, we aimed to summarise and synthesize the results of existing studies regarding the effects of AE only on balance, gait, functional mobility, and QoL in PD, providing more comprehensive information about each of these studies. We also sought to describe the similarities and differences between different AE protocols included in numerous systematic reviews in the literature. A graphical representation of this article can be seen in Figure 1.

Methods

This umbrella review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidance [34] (Supplementary Appendix 1)and the protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023386878).

Search strategy

A comprehensive literature search was conducted in collaboration with an expert librarian to identify systematic reviews investigating effects of AE on balance, gait, functional mobility, and QoL in individuals with PD. Six different databases were searched (Pubmed/MEDLINE, PEDro, Scopus, Cochrane Library, Embase, and CINAHL) from inception to June 28, 2024. The search was limited to systematic reviews, reviews, or meta-analyses. Identified articles were downloaded and archived to Mendeley (v2.83.0, Elsevier). A manual search was undertaken in the reference lists of included articles to identify articles not published in the selected databases. Full search strategies and the results of each database are provided in Supplementary Appendix 2. The PICO (Population, Intervention, Comparison, Outcome) method was used to frame this review. *Population:* reviews involving %100 PD patients, regardless of gender or disease severity. *Intervention*: reviews assessing the effects of AE. *Comparison*: reviews that compared AE with no treatment,

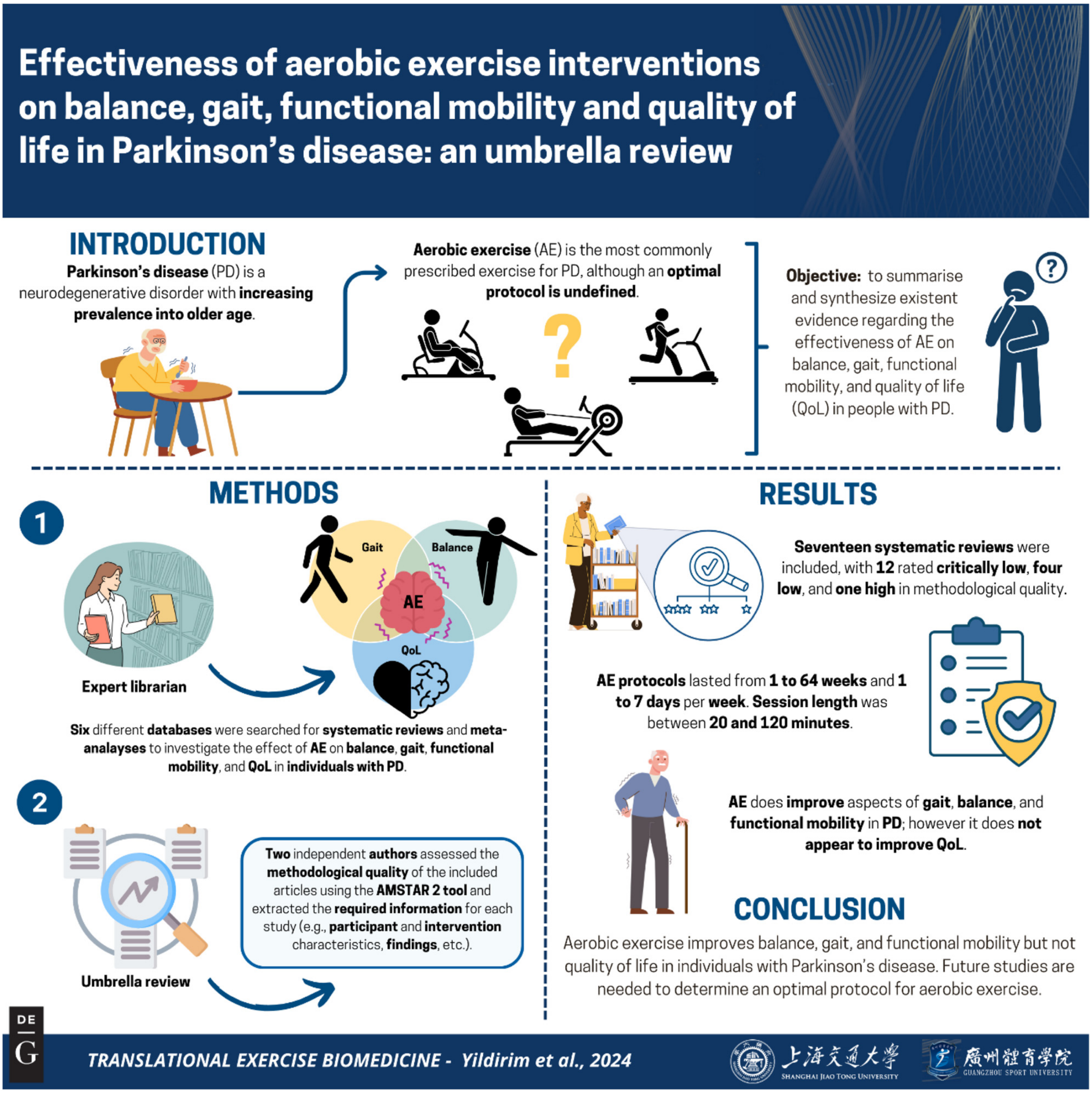

Figure 1: Graphical representation of this study. Key points [1]: The optimal prescription of aerobic exercise for people with Parkinson's disease is not well established [2]. Compiling data from 17 systematic reviews, aerobic exercise appears to improve balance, gait, and functional mobility but not quality of life in individuals with Parkinson's disease [3]. Given the heterogeneity in intervention design across studies, future studies directly comparing frequency, intensity, time and type of aerobic exercise are needed to determine an optimal protocol for people with parkinson's disease. Figure created with BioRender.

usual care, or any other exercise interventions. *Outcomes*: balance, gait, functional mobility, and QoL regardless of the measure. Articles were included if they were: systematic reviews with or without meta-analysis and were published in the English language. No exclusions were made on the basis of publication date, country, care setting, or age/sex of participants. Articles were excluded if they were published in a language other than English, did not investigate AE, or if they included participants with neurological conditions other than PD, comprised animal studies, were dissertations or theses, or were not published in a peer-reviewed journal.

Study selection

Screening of initial search results was carried out independently by two reviewers. The results of the search were transferred to Rayyan (Rayyan.ai Systems Inc.), where duplicates were removed. Then, titles and abstracts of remaining articles were reviewed against the eligibility criteria detailed above. If the abstract and title did not provide enough information for the authors to determine whether the review was eligible, the full-text was retrieved and evaluated. Following this, the full-text of remaining articles were thoroughly evaluated. Two independent authors were blinded to each other's decisions throughout the screening process. Disagreements were resolved through discussion between the two main reviewers and the opinion of a 3rd reviewer sought where disagreements could not be resolved.

Data extraction

Two reviewers independently extracted the required information using a pre-structured data extraction form summarizing: a) review details (authors' names, year of publication), b) participant characteristics (number, age, disease level, and disease duration), c) intervention characteristics (type, intensity, duration, and frequency) and comparator, d) number and type of included studies, e) outcomes, f) outcome measures, and g) findings.

Quality assessment

Two independent authors assessed methodological quality using the Assessment of Multiple Systematic Reviews 2 (AMSTAR 2); a tool to assess the quality of systematic reviews involving randomised (RCTs) or non-randomised controlled trials (NRCTs) based on 16 items [35]. Seven domains are considered critical to rate the methodological quality of the review, which are: i) Protocol registered before commencement of the review (item 2), ii) Adequacy of the literature search (item 4), iii) Justification for excluding individual studies (item 7), iv) Risk of bias from individual studies being included in the review (item 9), v) Appropriateness of meta-analytical methods (item 11), vi) Consideration of risk of bias when interpreting the results of the review (item 13), and vii) Assessment of presence and likely impact of publication bias (item 15). An AMSTAR 2 grade can be critically low, low, moderate, or high depending on how many critical and non-critical weaknesses are identified. A high rating means 'no or one non-critical weakness' and a moderate rating means 'more than one non-critical weakness'. A review is rated as 'low' if it has one critical weakness and as 'critically low' if it has more than one critical weakness [35]. Any disagreement in quality assessment between reviewing authors was resolved through discussion and the opinion of a 3rd reviewer where disagreement could not be resolved.

Assessment of study uniqueness

The eligible reviews were screened for overlapping primary studies using the Corrected Covered Area (CCA) method [36]. The following formula is used for calculating this CCA: (N-r)/(r*c-r), where N is the total number of times primary publications appeared in reviews, r is the number of unique primary publications, and c is the number of systematic reviews included in the umbrella review. A CCA of 100 % means that all of the reviews that were part of our umbrella review had the same primary research while a CCA of 0 % means that all of the primary studies in our umbrella review were completely unique. A classification of the degree of overlap is included with the formula; 0–5 % is regarded as "slight overlap", 6–10 % as "moderate overlap", 11–15 % as "high overlap", and >15 % as "very high overlap".

Data synthesis

Tables were used to synthesize data. A narrative synthesis approach was employed to present an overview of the results due to heterogeneity of outcome measures, intervention protocols, and participant characteristics in the included systematic reviews.

Results

Study selection

Our search identified 4,182 articles from six different databases and one additional review through the screening of reference lists of the included systematic reviews. After removing duplicates, title and abstract screening was performed on 2,736 papers, from which 2,618 were excluded. 101 of the remaining 118 articles were excluded at full-text review, leaving 17 systematic reviews for inclusion in the final analysis (Figure 2).

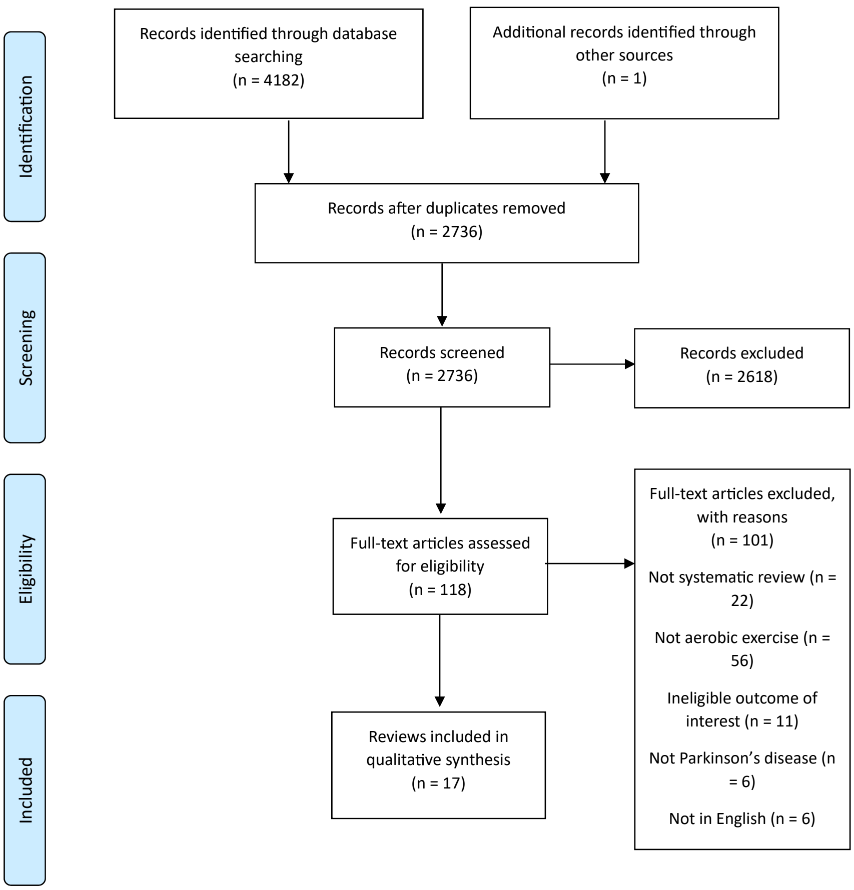

Figure 2: PRISMA flow diagram. From: Moher D, liberati A, tetzlaff J, Altman DG, the PRISMA group (2009). *P*referred *r*eporting *i*tems for *s*ystematic reviews and *m*eta-*a*nalyses: The PRISMA statement. PLoS med 6 (6): e1000097. doi:10.1371/journal.pmed1000097. For more information, visit www.prisma-statement.org.

Quality assessment

Only one review was rated as high quality, four as low, and 12 as critically low quality (Table 1). The quality requirements of items 1 (Did the research questions and inclusion criteria for the review include the components of PICO (Population, Intervention, Comparator, Outcome)?) and 16 (Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?) were fully met by all included reviews. All reviews fully or partially met the requirements of item 8 (Did the review authors describe the included studies in adequate detail?). Item 9 (Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?) was reported in 16 reviews out of 17 reviews. The majority of articles (16 out of 17) failed to report their source of funding (item 10).

Characteristics of included reviews

Characteristics of the included reviews are summarised in Table 2. The 17 included systematic reviews were conducted between 2014 and 2023. The mean number of included original studies was thirteen (range: 4–36). 13 reviews included only RCTs while four included both RCTs and NRCTs. Five reviews had AE sub-group analysis and the remaining 12 focused on AE without sub-categorisation.

The total number of participants was 4,236 across 114 primary studies. The sample size of included reviews ranged from 221 [39] to 1,443 [48] in the 16 reviews where this was reported. The average age of participants reported in the reviews ranged from 50 to 75 years in the 14 reviews where this was reported. The disease stage of participants was between Hoehn and Yahr (H&Y) stages 1–3 for the majority of reviews (n=11), although four reviews also included participants with H&Y stage 4. Two reviews did not provide any information on the disease stages of participants [44, 45]. Disease duration was between 0.3 and 18.1 years across the 11 reviews that reported this.

Ten reviews included AE without any limitation to modality (mixed modalities included) as the intervention. Three reviews focused on only Nordic walking [31, 39, 40], two focussed on treadmill walking and one on cycle ergometry [37, 41, 43], respectively. One review directly compared cycle ergometry with Nordic and downhill

Table 1: Quality assessment of included systematic reviews.

Yes	(green)
No	(red)
Partially yes	(yellow)
No meta-analysis conducted	(light blue)

	Zhen et al. 2022 [32]	Tiihonen et al. 2021 [37]	Schootemeijer et al. 2020 [38]	Rodríguez et al. 2021 [29]	Cugusi et al. 2017 [39]	Salse-Batán et al. 2022 [31]	De Santis and Kaplan 2020 [40]	de Oli-viera et al., 2021 [41]	Shu et al. 2014 [42]	Li et al. 2021 [30]	Mehrholz et al. 2015 [43]	Alves Da Rocha et al. 2015 [44]	Chen et al. 2020 [45]	Zhou et al. 2022 [46]	Lamotte et al. 2015 [47]	Zhang et al. 2023 [48]	Yang et al. 2023 [49]
1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Partially yes	Yes	No	No	No	Partially yes	Yes	Partially yes	Partially yes	No	Yes	No	Partially yes	Yes	No	Yes	Yes
3	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	Yes	Yes	No	No	No	Yes	Yes
4	Partially yes	No	No	Partially yes	Partially yes	No	Partially yes	Partially yes	No	Partially yes	Partially yes	Partially yes	Partially yes	Partially yes	No	Partially yes	Partially yes
5	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	No	No	No	No	Yes	No	Yes	Partially yes	Yes	No	Yes	No	No	No	No	No	No
8	Partially yes	Yes	Partially yes	Partially yes	Partially yes	Yes	Yes	Partially yes	Partially yes	Partially yes	Yes	Partially yes	Partially yes	Partially yes	Yes	Partially yes	Partially yes
9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
10	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No
11	Yes	Yes	Yes	No meta-analysis conducted	No meta-analysis conducted	Yes	Yes	No meta-analysis conducted	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
12	Yes	Yes	Yes	No meta-analysis conducted	No meta-analysis conducted	No	Yes	No meta-analysis conducted	No	No	Yes	No	Yes	Yes	No	No	Yes
13	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	No	No	Yes
14	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes
15	No	Yes	Yes	No meta-analysis conducted	No meta-analysis conducted	No	No	No meta-analysis conducted	No	Yes	Yes	No	Yes	Yes	No	No	Yes
16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Overall	Critically low	Critically low	Critically low	Critically low	Critically low	Critically low	Low	Critically low	Critically low	Critically low	High	Critically low	Low	Low	Critically low	Critically low	Low

Table 2: Characteristics of included systematic reviews. N, number of participants in original studies; DS, disease stage; DD, disease duration; H&Y, hoehn and yahr scale; AE, aerobic exercise; D, duration; F, frequency; I, intensity; T, time of the session; FRT, functional reach test; BBS, berg balance scale; TUG, timed up and go test; COP, centre of pressure; 6MWT, six-minute walking test; 10Mwt, ten-meter walking test; PDQ-39, parkinson's disease questionnaire; LRI, locomotor rehabilitation index; CS-PFP, the continuous scale-physical functional performance test; QoL, quality of life; RCTs, randomised control trials; UPDRS, unified parkinson's disease rating scale; NR, not reported; HRmax, heart rate maximum; NRCTs, non-randomised control trials; HRR, heart rate reserve; IGs, intervention groups; CGs, control groups.

First author, year	Included studies': number and type	Participants details (total number, age range, disease duration, H&Y stage)	Intervention protocols	Comparison	Outcome measure, s	AMSTAR 2 overall score	Findings
Zhen et al. 2022 [32]	20 studies, all RCTs	N: 450 in the IGs and 352 in the CGs, DS: Eighteen trials with H&Y 1–3; two trials with H&Y 1-4 Age: The mean age range was between 57.6 and 74 years old DD: NR	AE D: 3 weeks to 6 months T: 20–90 min sessions F: 2–5 sessions per week (the majority was 2–4)	no intervention, usual care, normal daily activities, and conventional medication	Balance (BBS and TUG) Gait (step length, gait speed, and cadence) QoL (PDQ-39)	Critically low	BBS and TUG are significantly improved. Step length and gait speed are significantly improved but not cadence. No significant effects on QoL
Tiihonen et al. 2021 [37]	22 studies, both RCTs and NRCTs	N: 505 DS: The mean H&Y was 2.06 in IGs and 2.04 in CGs. Age: The mean was 64.3 in IGs and 64.4 in CGs. DD: The mean duration was 6.4 in IGs and 6.5 in CGs.	Bicycling D: 1–12 weeks (average of 5.3) T: NR F: 1–5 sessions per week	Any treatment that did not include cycling (no more detail)	Balance (NR) Gait (6MWT, step length, gait speed, and cadence) QoL (PDQ-39)	Critically low	Balance is significantly improved. 6MWT and gait speed are significantly improved but cadence and step length are not. Overall QoL is significantly improved.
Schootemeijer et al. 2020 [38]	17 studies, all RCTs	N: 900 (ranging from 8 to 130) Age: NR DS: H&Y majority 1–3 (a few studies with 1–2, 1.5–3 and 2–3) DD: NR	AE (with at least 60 % of HRmax and lasting at least 4 weeks) D: 5 weeks to 16 months (the majority was 12 weeks) F: 2–7 times a week (the majority was 3–4)	Education class, conventional physiotherapy, flexibility, waitlist, usual care or strength exercises	QoL (PDQ-39)	Critically low	No significant improvement on QoL at the post-intervention assessment.
Rodríguez et al. 2021 [29]	7 studies, both RCTs and NRCTs	N: 419 (ranging from 13 to 130) Age: The mean ranged between 58 and 69.8 years old DS: H&Y 1–2 in three studies, 1–3 in two studies, 2–3 in one study	Vigorous AE (≥77 % HRmax, 60 % HRR, 64 % VO2max, or≥14 RPE) D: 8–26 weeks F: 3–4 times a week T: 25–60 min per session	Light or moderate-intensity AE or education classes, flexibility, resistance, or relaxation exercises	Balance (TUG, mini-BEST, force plate) Gait (gait speed) QoL (PDQ-39)	Critically low	Balance was not improved significantly. Gait is not affected significantly. QoL is improved in only high-intensity AE groups when compared to non-exercise control groups but not when compared to moderate or light-intensity AE.

Table 2: (continued)

First author, year	Included studies': number and type	Participants details (total number, age range, disease duration, H&Y stage)	Intervention protocols	Comparison	Outcome measure, s	AMSTAR 2 overall score	Findings
Cugusi et al. 2017 [39]	6 studies, all RCTs	N: 221 Age: The mean range was between 50 and 67.3 years old DD: The mean was between 1.5 and 7 years DS: H&Y 1–3 in four studies, 2–3 in one study, and 1–4 in one study	Nordic walking F: 2–5 days a week (an average of 2.8) D: 4–24 weeks (an average of 10.8)	Treadmill, walking, LSVT, flexibility, strength training or conventional care	Balance (TUG and BBS) Gait (10mWT) QoL (PDQ-39)	Critically low	In 4 of 6 studies, NW significantly improved balance and gait. QoL had contrasting results (improved in one study, no change in one study.
Salse-Batán et al. 2022 [31]	12 studies, all RCTs	N: 498 (with a range between 20 and 90) Age: The mean age range was 50–75 years old. DS: H&Y ranged between 1.5 and 4. DD: Between 5.1 and 7.8 years in six studies; between 17.98 and 71.98 months in three studies.	Nordic walking D: 4–24 weeks F: 2–5 times a week (2 times was the most frequent one) T: 35–90 min. I: ranging between 60 and 80 % of HRR in five studies; speed progression in one study.	Treadmill, domestic training, free walking, standard rehabilitation or no exercise	Balance (BBS) Gait (walking ability) QoL (PDQ-39) Functional mobility (TUG)	Critically low	Balance is significantly improved compared to baseline but not other therapies. Gait is improved significantly compared to baseline and other therapies. Significant improvement in QoL at post-intervention in 3 studies out of 5. Functional mobility is improved compared to baseline and other therapies.
De Santis and Kaplan 2020 [40]	13 studies, both RCTs and NRCTs	N: 318 (182 in IGs and 136 in CGs) Age: The mean age range was between 58 and 73 DS: The H&Y was mainly 1-3 DD: Between 1.5 and 8 years.	Nordic walking T: mostly 60 min F: 2–3 times a week D: 6–12 weeks	Free walking without poles, structured physiotherapy program BIG, unsupervised home exercises, flexibility and relaxation training, and standard medical care	Balance (TUG, BBS, COP) Gait (walking endurance and speed) QoL (PDQ-39) Functional mobility (LRI)	low	Balance is improved compared to baseline and control groups. Gait is improved compared to baseline and control groups. QoL is improved compared to baseline and control groups Mobility is improved compared to baseline and control groups
de Oliviera et al., 2021 [41]	10 studies (all RCTs)	N: 411 (ranging from 14 to 128) DD: The mean ranged from 4.8 to 8.9 years in IGs and 4.3–8.5 years in CGs. DS: The H&Y was 1–3 in four studies, 1 to 2 in two studies, 1.5 to	Treadmill in eight studies and walking in two studies. I: from 60 to 85 % of HRmax in treadmill studies. One walking study used the intensity from 60 to 80 % of HRmax.	Usual care, flexibility and relaxation, conventional physiotherapy, conventional care, low intensity exercise and maintaining daily physical activities.	Balance (BBS) Gait (speed, cadence, and length) QoL (PDQ-39) Functional mobility (TUG)	Critically low	Balance is not improved significantly. Speed and stride length are improved significantly but not cadence. No significant improvement in QoL Functional mobility is significantly improved.

Table 2: (continued)

First author, year	Included studies': number and type	Participants details (total number, age range, disease duration, H&Y stage)	Intervention protocols	Comparison	Outcome measure, s	AMSTAR 2 overall score	Findings
		2.5 in two studies, and 2 to 3 in two studies. Age: The mean was 63.5 ± 2.6 years in IGs and 63.5 ± 1.7 years in CGs.	T: between 20 and 70 min. F: from 2 to 4 times per week. D: from 4 to 26 weeks.				
Shu et al. 2014 [42]	18 studies (all RCTs)	N: 901 Age: The mean was 67 ± 3.3 years. DD: The mean was 6.4 ± 2.7 years. DS: Fourteen studies with H&Y 1–3 and two studies with H&Y 1–4. 2 studies did not report.	AE I: NR F: 2–7 times a week. (3 was the most frequent) D: between 3 weeks and 16 months. T: 20–70 min	no intervention, usual care, stretching, resistance exercises, physical therapy, and other exercise	Balance (BBS, FRT) Gait (6MWT, stride/step length, gait speed, cadence, and TUG) QoL (PDQ-39)	Critically low	Balance is significantly improved. Gait measurements (except cadence) showed significant improvements There was no significant change in QoL
Li et al. 2021 [30]	9 studies (all RCTs)	N: 444 (227 in IGs and 217 in CGs) Age: The mean was between 59 and 68 years old. DS: Three studies with H&Y 1–2 and five studies with H&Y 1–3. 1 study did not report. DD: The mean ranged from 0.3 to 8.89 years.	Moderate-intensity AE D: from 8 weeks to 16 months. F: 2–7 sessions per week. (The majority was 2–3) T: 20–90 min. I: moderate (the HRR ranged from 50 to 80 %)	Routine or home-based exercises	Balance (TUG) Gait (6MWT) QoL (PDQ-39)	Critically low	Balance is improved significantly. Gait is improved significantly. QoL was not improved overall. After having a subgroup analysis, the treadmill group improved QoL more than the controls.
Mehrholz et al. 2015 [43]	18 studies (all RCTs)	N: 623 Age: The mean was between 58 and 74 years DS: Most studies with H&Y 1–3. DD: The mean was between 1 and 13 years.	Treadmill training I: any intensity F: 3–7 days a week. (3 was the most frequent) D: 4–24 weeks. T: 20–60 min.	Overground walking, usual care, robotic gait training, no exercise, traditional physiotherapy, stretching and resistance exercises	Gait (gait speed, cadence, stride length, walking distance)	High	Gait speed and stride length are improved significantly but cadence and walking distance are not affected.
Alves Da Rocha et al. 2015 [44]	4 studies (subgroup) (both RCTs and NRCTs)	No details since this is a subgroup analysis of AE.	Cycle ergometer, Nordic walking, downhill walking F: 1–3 days a week. T: 30–60 min.	No treatment or conventional physiotherapy	Balance (NR) Gait (NR) QoL (NR) Functional mobility (NR)	Critically low	Cycle ergometer significantly improved functional mobility, gait, and balance but there was no change in QoL. Nordic and downhill walking significantly improved gait, functional mobility, and QoL.

Table 2: (continued)

First author, year	Included studies': number and type	Participants details (total number, age range, disease duration, H&Y stage)	Intervention protocols	Comparison	Outcome measure, s	AMSTAR 2 overall score	Findings
Chen et al. 2020 [45]	5 studies (sub-group) (all RCTs)	N: 398 Age: The mean ranged between 60 and 70.2 years old. DD: The mean ranged from 5.7 to 7.7 years. One study did not report.	AE F: 2–5 days a week. D: 3–12 weeks. T: 30–120 min.	Control groups maintained their normal lifestyle and current levels of physical activity, took no extra exercise or training	QoL (PDQ-39)	low	QoL was significantly improved by AE.
Zhou et al. 2022 [46]	10 studies (subgroup) (all RCTs)	N: 418 DS: Three studies with H&Y 1–2; five studies with H&Y 1–3, one study with H&Y 1–1.5, one study with UPDRS>30 AGE: The mean ranged from 61.8 to 67.4 years old. 3 studies did not report.	AE D: ranged from 4 weeks to 6 months. F: 2–4 days a week. I: Low, moderate, and high intensities were compared	Usual care, no intervention or stretching training	Gait (6MWT, 10mWT) QoL (PDQ-39) Functional mobility (TUG)	low	AE improved 10mWT significantly (except low-intensity AE with>12 weeks) 6MWT was significantly improved by low-intensity AE (with>12 weeks). (Other durations and intensities also improved but not significantly) QoL was significantly improved by low and moderate-intensity AE with<6 weeks. TUG significantly improved by high-intensity AE with>12 weeks (other duration and intensities also improved but not significantly).
Lamotte et al. 2015 [47]	8 studies (all RCTs)	N: 338 (ranging from 8 to 121) DS: H&Y 1–3 in six studies and UPDRS motor score<35 in one study and mean UPDRS with 49 in one study. AGE: NR DD: NR	AE D: 6–64 weeks F: 60–180 min per week I: HRmax>60 % at least with a target HRmax between 60 and 85 %.	No exercise, other exercise types, AE with different intensities or daily physical activities.	Gait (speed, step length, cadence, double support time, base of support, distance) Balance (single limb stance and FRT) Functional mobility (TUG, CS-PFP, and a variety of timed measures including U-turns, turning around a chair, stair climbing, and arising from a chair) QoL (PDQ-39)	Critically low	Gait speed and double support time were improved but not other measures of gait. Single limb stance was significantly improved on the right foot but not the left. FRT did not improve significantly. TUG and CS-PFP did not improve significantly. However, other combined measure was improved significantly. No significant change in QoL.

Table 2: (continued)

First author, year	Included studies': number and type	Participants details (total number, age range, disease duration, H&Y stage)	Intervention protocols	Comparison	Outcome measure, s	AMSTAR 2 overall score	Findings
Zhang et al. 2023 [48]	36 studies (sub-group)(all RCTs)	N: 1,443 (ranging from 17 to 130) DS: The mean H&Y ranged from 1.5 to 3. Age: The mean age range was between 58.30 and 73.6 years. DD: The mean DD ranged between 2.5 and 18.10 years.	Nordic walking, treadmill, AE F: 2–7 days a week. D: 4–24 weeks. T: 25–120 min. I: NR	Control, body-weight supported treadmill, qigong, resistance training, multi-component training, virtual reality, balance and gait training, stretching	Gait (TUG, cadence, stride length, 6MWT)	Critically low	Gait parameters, except cadence, were improved.
Yang et al. 2023 [49]	5 studies (sub-group)(all RCTs)	N: 238 (ranging from 20 to 128) DS: The mean H&Y ranged from 1.66 to 2.4. Age: The mean age range was between 57.6 and 68.1 years. DD: The mean DD ranged between 0.73 and 8.89 years.	AE F: 2–4 days a week. D: 4–26 weeks. T: 30–50 min. I: any intensity	No training, maintaining exercise habits, education, and dopamine.	Gait (speed and 6MWT) Balance (BBS and mini-BEST) Functional mobility (TUG)	Low	6MWT is improved after AE but not gait speed. Balance is improved after AE training. AE had no significant effect on functional mobility.

walking [44]. Approximately half of the included reviews (n=8) did not report any information regarding the intensity of AE. Of those that did report intensity, moderate-intensity exercise was the focus of four reviews (defined by heart rate in all instances [30, 38, 41, 47] and high-intensity exercise was the focus of two reviews (defined by heart rate in one, and maximal oxygen consumption, rate of perceived exertion (RPE) or heart rate in the other [29, 31]. Two reviews stated that they included any intensity of AE [43, 49]. One article directly compared low, moderate, and high-intensity AE [46]. The frequency of intervention ranged from one to seven days per week, with most of the reviews reporting two to four sessions per week. The duration of the intervention was between one and 64 weeks. The sessions lasted between 20 and 120 min. Where stated, shorter duration sessions were preferred to longer ones by people with PD. Five reviews did not report any information regarding session length, while intervention duration was not mentioned in only one review [44].

The effects of aerobic exercise interventions

The effects of AE on balance were assessed in 12 reviews. The outcome measures for balance varied, with a range of tests including Berg Balance Scale (BBS), Timed Up and Go test (TUG), mini-BEST (Balance Evaluation Systems Test), force plate, Centre of Pressure (COP), Functional Reach test (FRT), and single limb stance. The most commonly used measures were BBS and TUG, assessed in seven and five of the 12 reviews, respectively. Two reviews did not report what measure was used for balance [37, 44]. Seven reviews stated that AE significantly improved balance compared to baseline and control groups (with a small effect size (ES) in one review, a moderate ES in two reviews, and a large ES in two reviews, where reported). One review found that AE was beneficial in improving balance compared to baseline (with a large ES), but not when compared to other therapies [31]. Another review conducted by Lamotte et al., used two different balance measurements (single limb stance and

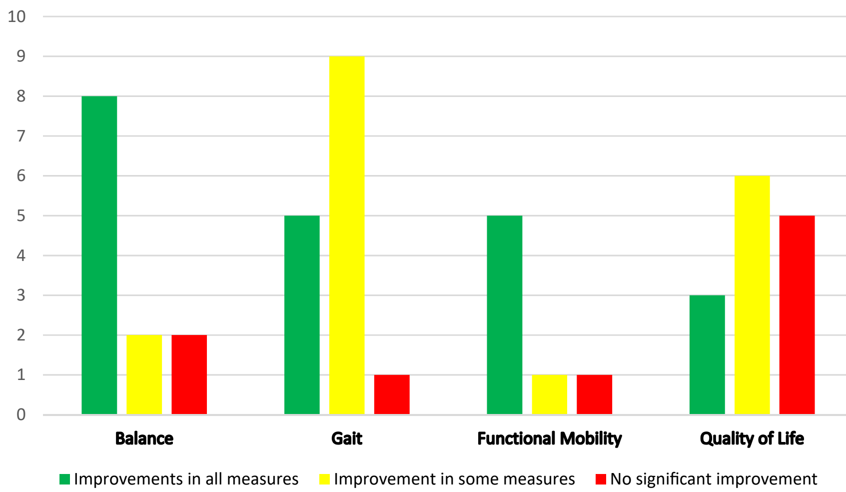

Figure 3: The effects of aerobic exercise interventions on outcomes in people with Parkinson's disease. Considering gait, cadence was the most common parameter that did not significantly improve.

FRT) [47] reporting single limb stance to be significantly improved in the right leg only and that FRT did not change after AE. In a review that included Nordic walking as their intervention, balance was significantly improved in four of six original studies [39]. However, two other reviews concluded that AE interventions did not have any significant effect on balance in PD [29, 41]. One of these reviews included only mild to moderate stages of PD patients and most of the primary studies had relatively short intervention periods (<12 weeks) [41]. The other study that stated AE did not improve balance measures focused on high-intensity AE interventions (RPE>15, Heart rate reserve>70 %, and Heart rate maximum>80 %) [29] (Figure 3).

Gait was the most commonly evaluated outcome in the PD population performing AE, with 15 reviews reporting this. The outcome measures that were used to assess gait included step length, cadence, six-minute walk test (6MWT) distance, gait speed, ten-meter walking test (10 mWT) time, walking ability, walking endurance, stride length, TUG, walking distance, double support time, and base of support. Gait speed and cadence were the most commonly used assessment methods reported in nine and seven reviews, respectively. Five reviews reported significant improvements (with a large ES in one review and a moderate ES in two reviews; where reported) in aspects of gait following AE. Three out of these five reviews had a longer duration of AE (>12 weeks). Also, the majority of five reviews included Nordic walking, where AE modality may have played an important role in gait measures' improvements. The remaining 10 reviews showed that not all gait parameters benefitted from AE interventions (Table 2). Cadence did not significantly improve after AE in seven reviews, similar to step length, gait speed, and walking distance which also did not improve according to two reviews (Figure 3).

Functional mobility was assessed in seven reviews. TUG, Locomotor Rehabilitation Index (LRI), the Continuous Scale-Physical Functional Performance test (CS-PFP), U-turns, turning around a chair, stair climbing, and rising from a chair were the outcome measures employed in these reviews. The most commonly used measurement was TUG, reported in five reviews. Five reviews reported that AE was beneficial (with a moderate ES in one review and a small ES in two reviews; where reported) in improving the functional mobility of people with PD. One of these reviews which also compared intensities of AE reported that it was higher-intensity AE with a longer duration (12+ weeks) which significantly improved TUG [46]. Another review reported that AE did not affect TUG or CS-PFP, but that a combined measure (including U-turns, turning around a chair, stair climbing, and arising from a chair) was significantly improved in individuals with PD after AE [47]. The last review highlighted that AE had no significant effect on functional mobility, whereas the other exercise types (resistance, mind-body, balance and gait training) were effective [49] (Figure 3).

QoL was assessed in 14 reviews. The Parkinson's Disease Questionnaire (PDQ-39) was the most common measure of QoL used in 13 of the 14 studies. Only three reviews reported that QoL was improved (with a small ES in two reviews; where reported) after AE interventions [37, 40, 45], while five reviews found QoL was not affected by AE [32, 38, 41, 42, 47]. Two reviews stated no change in QoL after all AE interventions combined but sub-group analysis found that treadmill, Nordic, and downhill walking did have a positive effect on QoL in people with PD [30, 44]. Further, two reviews compared different intensities of AE on QoL [29, 46]. One of these reported high-intensity AE as associated with promoting improvements in QoL, whereas the other stated that only high-intensity AE did not affect QoL in individuals with

PD. Two further reviews had contrasting results on the effects of AE on QoL [31, 39] (Figure 3).

Overlapping and unique studies

The 17 systematic reviews in our umbrella review included 114 primary studies. Of 114, 72 primary studies were unique. The CCA for these 17 reviews was 5.81 %, indicating a moderate degree of overlap. A Matrix of Evidence table to demonstrate the degree of overlap between primary studies in the included reviews is provided in Supplementary Appendix 3. The highest overlap was 38.5 % (between Cugusi et al. 2017 [39] and Salse-Batán et al. 2022 [31]) (Figure 4).

Discussion

This umbrella review provides an overview of the effectiveness of AE interventions on gait, balance, functional mobility, and QoL in people with PD. There are just five umbrella reviews in the literature assessing the effects of physical therapy interventions on PD populations, four of which have not focused on AE, despite its commonplace in exercise prescription for this patient group. Only Padilha and colleagues included AE in their umbrella review, however, they only provided a summary paragraph regarding the effects of AE in PD and did not discuss the effects of different AE protocols in depth [33].

Our comprehensive literature search allowed the inclusion of 17 reviews synthesising the evidence from relevant trials, revealing that (i) AE interventions may be beneficial for eliciting improvements in gait, balance, and functional mobility for people with PD, but (ii) it is unclear whether AE can improve QoL in PD. Despite the inclusion of over 8,000 participants, it should be acknowledged that the data underpinning this review was based on heterogeneous AE interventions, with marked variation in AE frequency, duration, modality, and intensity: making it difficult to draw firm conclusions on optimal AE intervention protocols for each outcome.

Balance is an important outcome for people with PD since many report difficulties with this, and it is linked to reduced functional mobility, QoL, and an increased risk of falls [50, 51]. The majority of reviews included herein that reported on balance indicate that AE can improve balance measures in individuals with PD. Balance scores (although based on various assessments) improved after AE *per se*, and

	Zhang et al., (202	Yang et al. (2023)	Zhou et al. (2022)	Chen et al. (2020)	Alves da Rocha et al. (2015)	Mehrholz et al. (2015)	Shu et al. (2014)	De Oliviera et al. (2021)	De Santis and Kaplan (2020)	Salse-Batan et al. (2022)	Cugusi et al. (2017)	Rodriguez et al. (2021)	Schootemeijer et al. (2020)	Tiihonen et al. (2021)	Zhen et al. (2022)	Li et al. (2021)
Yang et al. (2023)	5.1%															
Zhou et al. (2022)	12.2%	15.4%														
Chen et al. (2020)	2.5%	0.0%	7.1%													
Alves da Rocha et al. (2015)	2.6%	0.0%	0.0%	0.0%												
Mehrholz et al. (2015)	17.4%	9.5%	12.0%	4.5%	4.8%											
Shu et al. (2014)	12.5%	9.5%	7.7%	4.5%	0.0%	33.3%										
De Oliviera et al. (2021)	15.0%	15.4%	33.3%	7.1%	7.7%	16.7%	12.0%									
De Santis and Kaplan (2020)	8.9%	5.9%	4.5%	0.0%	6.3%	0.0%	3.3%	9.5%								
Salse-Batan et al. (2022)	6.7%	6.3%	4.8%	0.0%	0.0%	0.0%	3.4%	10.0%	19.0%							
Cugusi et al. (2017)	10.5%	10.0%	6.7%	0.0%	0.0%	0.0%	4.3%	14.3%	35.7%	38.5%						
Rodriguez et al. (2021)	7.5%	20.0%	13.3%	0.0%	0.0%	8.7%	8.7%	6.3%	0.0%	0.0%	0.0%					
Schootemeijer et al. (2020)	20.5%	15.8%	28.6%	0.0%	0.0%	9.4%	12.9%	17.4%	3.4%	3.6%	4.5%	20.0%				
Tiihonen et al. (2021)	7.3%	3.7%	10.0%	0.0%	0.0%	0.0%	0.0%	3.1%	2.9%	2.9%	3.6%	0.0%	5.3%			
Zhen et al. (2022)	14.6%	9.1%	7.4%	4.3%	0.0%	8.8%	19.4%	20.8%	0.0%	0.0%	0.0%	8.3%	20.0%	2.4%		
Li et al. (2021)	12.5%	16.7%	11.8%	0.0%	0.0%	0.0%	3.8%	26.7%	4.8%	5.0%	7.1%	14.3%	13.0%	6.7%	16.7%	
Lamotte et al. (2015)	10.0%	8.3%	12.5%	0.0%	0.0%	13.0%	18.2%	5.9%	0.0%	0.0%	0.0%	15.4%	31.6%	0.0%	3.8%	6.3%

136	=	Total nodes (pairs of reviews)
61	=	Slight overlap (<5%)
31	=	Moderate overlap (5% to <10%)
19	=	High overlap (10% to <15%)
25	=	Very High overlap (≥15%)

Figure 4: Graphical representation of overlap for OVErviews: GROOVE tool.

more specifically after Nordic walking and cycling [31, 32, 37]. The 2018 Physical Activity Guidelines Advisory Committee (PAGAC) Scientific Report supports these findings, emphasising the importance of AE for improving balance in individuals with PD [52]. Only two of the 12 reviews which reported on balance did not find any significant improvement in balance after AE; both of which included high-intensity interventions [29, 41]. Therefore, it may be that training intensity is an important factor in determining if AE can elicit improvements in balance for people with PD, as moderate-intensity AE does appear more favourable [30]. Beyond intensity, there is also evidence to suggest that multi-component exercise protocols including balance exercises may be superior to AE alone, if the primary aim is to improve balance and reduce falls [53], supporting a multi-faceted and targeted approach to the management of PD.

Gait impairments are one of the key factors that reduce QoL for people with PD, with slower gait speed also increasing the risk of falls and complications [54, 55]. Five of the reviews included herein stated that all gait measurements were positively affected by AE interventions. Further, another nine included reviews reported that some, but not all, of the assessed gait parameters were improved. Cadence was the most common parameter *not* significantly improved by AE, with more favourable results for gait speed, step length, stride length, and 6MWT. This disparity across gait parameters may be explained by Pohl et al., who stated that the control mechanisms of cadence are not impaired in PD and that that gait hypokinesia seen in PD is associated with a lack of ability to produce large steps and not with cadence impairment [56]. Cadence may therefore not be the most appropriate outcome measure to assess intervention effectiveness in PD. Regarding intensity, only one review aimed to understand the impact of exercise intensity on gait speed, reporting no significant difference when high intensity AE was compared to moderate intensity [29]. High-intensity AE is likely not required to elicit improvements in gait speed [57] as it may be the rhythmic stimulation (i.e. external sensory input) of some AE modalities which elicit benefit in this parameter. For example, a mini review by Herman and colleagues showed treadmill exercise to be more beneficial than overground walking for gait improvements in individuals with PD. They suggested that treadmill training may elicit positive neural changes due to the paced and rhythmic motor commands of this mode of AE. Mechanistically, they suggested that movement on a moving platform (i.e., treadmill walking) provides external cueing that is mediated through proprioceptive and vestibular receptors which, in turn, generates repetitive sensory input to the central nervous system [58]. The suggestion of rhythmic AE being important for gait improvements in PD is also supported by another umbrella review focussed on AE and adjuvant rhythmic stimulation/cueing, which stated that AE combined with rhythmical auditory stimulation further improves gait-related outcomes in people with PD [59]. Collectively, it appears that AE can be a beneficial tool to improve gait parameters in individuals with PD, although cadence does seem to be an exception.

Functional mobility can be defined as the ability to move independently, effectively, and safely to manage required functional tasks and ADLs [60]. Reduced functional mobility is a common feature of PD and is directly affected by both motor and non-motor symptoms. Given the impact of this parameter on independence and QoL, this is often a primary target for rehabilitation in people with PD [61]. Somewhat surprisingly given its clear importance, functional mobility was the least assessed outcome in the included reviews when compared to gait, balance, and QoL. Of the studies that did assess this parameter (n=7), TUG was the most common measure and was reported in five reviews. Overall, most included reviews (n=5) found a significant improvement in functional mobility after AE interventions, although not necessarily via all measures [47]. The present umbrella review does support the use of AE to improve functional mobility, however duration and intensity appear to impact efficacy, especially for TUG. For example, a longer duration and high-intensity AE was suggested to be required to improve TUG in the systematic review of Zhou and colleagues [46]. This suggestion alongside the importance of AE modality, not only for functional mobility but also for the other important parameters outlined in this review, should be explored in more detail in the future.

QoL is a broad domain that is affected by not only motor symptoms but also by non-motor symptoms such as sleep, emotion, and cognition. The PDQ-39 questionnaire, a self-reported assessment consisting of eight domains (mobility, ADLs, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort) is widely used in people with PD [62]. This umbrella review confirms that there is unclear and inconsistent evidence regarding the effectiveness of AE on QoL, with most of the reviews included in this synthesis not reporting any significant improvements. However, this conflicts with the aforementioned mini-review conducted by Herman et al. [58], which demonstrated that long-term treadmill training can improved QoL in individuals with PD. This disagreement may be due to a lack of longer-term follow-up assessment in the articles included in our review, most of which also consisted of relatively short intervention periods compared to those in the review by Herman colleagues. Improvement in PDQ-39 score may not be discernible over short time periods due to the wide variety of dimensions mentioned above, each of which may have different temporal profiles of adaptation/and or may not be linear in nature. In support of this, other reviews have suggested that rehabilitation for people with PD should include different forms of exercise and medication for QoL improvement due to the different (internal and external) dimensions affecting it [63, 64].

Well-designed, suitably powered trials are still needed to further explore the optimal 'dose' of AE to improve physiological, psychological, and symptom-status in individuals with PD. To date, no study has directly compared the effect of different durations or frequencies of AE to elicit benefits; with very few studies available comparing different intensities of AE. There are also only two studies that compare different modalities of AE in PD [65, 66], despite mechanistic evidence to suggest differences even between different forms of the same modality (i.e., treadmill vs. overground walking). Larger trials should also include longer follow-up periods to explore the long-term effects of AE on PD symptoms. Moreover, people with PD have been found to have maintained their pedalling ability better than walking as the disease progresses [67]. As such, future studies should focus on the potential cycle-ergometry as an AE modality since this is largely overlooked in the literature. Finally, there is limited information on whether sex impacts the effectiveness of exercise interventions for management and symptom alleviation in individuals with PD. This needs further attention for optimised, personalised prescriptions to be developed.

Strengths and limitations

This was a comprehensive umbrella review summarising a breadth of evidence regarding the effectiveness of AE on outcomes deemed important to people with PD. We adhered to a pre-published protocol (PROSPERO: CRD42023386878) and utilised a recommended tool to assess the methodological quality of included reviews. Screening, selection, and quality assessment were done by two independent reviewers and by a third researcher when needed. Despite these strengths, limitations of this review include publication in the English language as a requirement, which may have increased the risk of selection bias. Secondly, it was not feasible to conduct a meta-analysis due to the heterogeneity of the literature. Finally, that the mean age of the participants ranged from 50 to 75 years in included reviews highlights a likely recruitment bias since the median age of onset in PD is 72 years, and this may affect the generalisability of our findings to real-world populations [68].

Summary and outlook

In summation, this umbrella review surmises that AE in people with PD may improve gait (except cadence), balance, and functional mobility. However, AE does not appear to improve QoL for individuals with PD. Moderate-intensity AE appears to have potential to improve PD outcomes, with some reviews reporting favourable outcomes with lower intensity exercise. Conversely, higher-intensity exercise may be needed for other outcomes. This needs to be better defined. Further, multi-component exercise programs may be more beneficial than AE alone for balance improvements in people with PD. However, to date, neither the optimal modality(s) or volume (session/programme duration and frequency) of AE for people with PD is known, irrespective of outcome of interest. Finally, the effectiveness of AE interventions on different disease stages (mild vs. moderate vs. severe) should be compared as there is insufficient information regarding this.

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Informed consent: Not applicable.
Author contributions: The review was designed by MCY, BEP, ALG, JC, JP, and RS. Running the search was completed by MCY. Data extraction was completed by MCY and HSE. Screening, selection, quality assessment, and reviewing records were done by MCY, HSE, and JC. The data were interpreted, and the manuscript was drafted by MCY. BEP, ALG, JC, JP, and RS reviewed and revised the manuscript. All authors read and approved the final manuscript.
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